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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,415	11/13/2006	Laszlo Czibula	2124.0070000	3182

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EXAMINER	
FIERRO, ALICIA LORETTA	

ART UNIT	PAPER NUMBER
4121	

MAIL DATE	DELIVERY MODE
01/22/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/550,415	CZIBULA ET AL.	
	Examiner	Art Unit	
	ALICIA L. FIERRO	4121	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

1. Claims 4-11 are pending in the instant application according to the *Amendments to the Claims*, filed on November 13, 2006.

Priority

2. The instant application is a national stage entry of PCT/HU2004/000026, filed March 23, 2004, which claims priority to Hungarian Patent document P0300761, filed March 24, 2003.

Information Disclosure Statement

3. No Information Disclosure Statement has been filed in the instant application. Applicants are reminded of their duty to disclose all information known to them to be material to patentability as defined in 37 C.F.R. 1.56.

Objections

4. The examiner objects to the specification for failure to comply with MPEP § 608.01(f). The specification does not include a reference to and brief description of the drawing(s) as set forth in 37 CFR 1.74.

Claim Rejections – 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. Claims 4-5 and 7-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,397,792 in view of U.S. Patent No. 6,689,755.

8. Please note that the word "pure" was not defined in the instant specification. As this concept can be defined in several different ways (for example, enantiomerically pure,

morphologically pure, or chemically pure), the examiner has taken "pure" to mean "morphologically pure" for purposes of prosecution on the merits.

9. Patent document '792 discloses methods of preparation of [R-(R*,R*)]-2-(4-Fluoropenyl)-,-dihydroxy-5-(1-methyl-ethyl)-3-phenyl-4-[phenyl-4-[(phenylamino) carbonyl]-1H-pyrrole-1-heptanoic acid, hemi calcium salt (atorvastatin calcium); this compound is the calcium salt of a compound of formula Ia-1 in column 20. See Example 1, column 25, lines 48-56 wherein calcium acetate is added to a solution of the sodium salt of the above compound. The solvent contains a mixture of water and *tert*-butyl methyl ether. The final product is isolated by filtration.

10. The reference differs from the instant claims insofar as it does not specifically teach that the final product is amorphous and it does not teach the use of lysine or arginine in the process.

11. The '755 patent teaches the use of zwitterion solutions as stabilizers for biologically active substances for the preparation of a fully amorphous and homogeneous product. Column 3, lines 42-3, state explicitly that the preferred zwitterions for this process are amino carboxylic acids, with lysine, arginine, and salts thereof, described as possible stabilizers. Because the product is fully amorphous, it is of high morphological purity.

12. One of ordinary skill in the art would be motivated to combine the method of preparing atorvastatin taught by '792 with the amino acid stabilizers disclosed in '755 because it is well known in the art that the amorphous form of atorvastatin calcium has better bioavailability than the various crystalline forms of the compound. It is therefore desirable to perfect a process for preparing fully amorphous atorvastatin for the purpose of improved therapeutic use. Thus, it

would be *prima facie* obvious to combine these two references with a reasonable expectation of success.

13. Claims 6 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,397,792 in view of U.S. Patent No. 6,689,755, as applied to claims 4-5 and 7-10 above, and further in view of U.S. Patent document US 2002/0183527 A1 (published 12/5/2002).

14. Please see paragraphs 8 and 10 for the applicable information disclosed in patent documents '792 and '755, respectively. Taken together, these references differ from the instant claims insofar as the do not specifically teach the organic solvents of claims 6 and 11.

15. The '527 document discloses a process for the preparation of amorphous atorvastatin from its various crystalline forms, or mixtures of crystalline and amorphous forms. In the first step of the preparation, atorvastatin is dissolved in a solvent in which it is soluble. Such solvents include polar solvents, either protic or aprotic, such as "low molecular alcohols" and ketones. Examples given include methanol, ethanol, and acetone.

16. One of ordinary skill in the art would be motivated to combine the method of preparing atorvastatin taught by '792 patent in conjunction with '755 patent, and the solvent choice of '527 patent since atorvastatin is known to be readily soluble in the solvents listed in '755. It would be desirable and obvious to use one of the solvents listed in '755. The Examiner asserts that one of ordinary skill in the art would have known that maximizing the solubility of atorvastatin salt in the reaction mixture would ultimately allow for more atorvastatin to be available to react, which would be likely to ultimately increase the product yield and additionally increase the reaction

rate. Thus, there would be *prima facie* obvious motivation to combine these three references with a reasonable expectation of success.

Conclusion

17. No claims are allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALICIA L. FIERRO whose telephone number is (571)270-7683. The examiner can normally be reached on Monday - Friday 8:00-5:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Patrick Nolan can be reached on (571)272-0847. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AF

/Patrick J. Nolan/
Supervisory Patent Examiner, Art Unit 4121